IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICANT	: Jackowski *et al.*
INVENTION	: **Complement C3 Precursor Biopolymer Markers Predictive of Type II Diabetes**
SERIAL NUMBER	: 09/993,287
FILING DATE	: November 23, 2001
EXAMINER	: Cook, Lisa V
GROUP ART UNIT	: 1641
OUR FILE NO.	: 2132.108

Mail Stop: RCE
Commissioner for Patents
P.O. Box 1450
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allowable subject matter of SEQ 1 and 2.

DECLARATION UNDER 37 CFR § 1.132

I, Ferris H. Lander, do hereby declare as follows:

1. I am a registered Patent Agent and am authorized to represent the inventor's and assignee in the application entitled **"Complement C3 Precursor Biopolymer Markers Predictive of Type II Diabetes"**, having U.S. Application Serial No. 09/993,287, filed November 23, 2001.

2. In the Advisory Action mailed on December 29, 2005, the Examiner maintained the Final Action. Specifically, the Examiner asserts that the figures do not show clear differential expression

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of the claimed sequences.

3. Applicants strongly disagree with the Examiner's determination and assert that the figures do provide clear differential expression of the claimed sequences (SEQ ID NOS:1-3).

4. The first figure attached hereto is entitled "DEAE 1(Elution) Normal vs. Diabetes Type II" and represents Figure 1 as originally filed. This figure was produced by scanning the original photograph of the gel. The claimed SEQ ID NOS:1 and 2 were obtained from samples analyzed in the gel shown in Figure 1.

At page 46, lines 8-11 of the instant specification as originally filed, SEQ ID NO:1 is identified as a fragment of the complement C3f precursor protein having a molecular weight of about 1212 daltons (1211.67 daltons). Figure 2, as originally filed, shows the characteristic mass spectral profile of SEQ ID NO:1 (see top left of figure for band number analyzed, D1(E)C3-2 and see top right of figure for molecular weight of the exemplified ion, 1211). Band 3-2, identified in lane 1 of the gel shown in Figure 1, is clearly labeled as containing complement C3f. Thus, it can be ascertained that the claimed SEQ ID NO:1 is a fragment of the complement C3f precursor protein weighing about 1212 daltons obtained from Band 3-2 of the gel as shown in Figure 1. Band 3-2 is immediately evident in all four normal samples (lanes 1-4, as read from the left, marked by circles) and clearly absent in all five diabetes Type II samples (lanes 5-9, marked by squares). * figure 1 L/C 2/17/06

At page 46, lines 11-13 of the instant specification as originally filed, SEQ ID NO:2 is identified as a fragment of the complement C3 precursor protein having a molecular weight of about 2173 daltons (2172.99 daltons). Figure 3, as originally filed, shows the characteristic mass spectral profile of SEQ ID NO:2 (see top left of figure for band number analyzed, D1(E)C3-2 and see bottom right of figure for molecular weight of the exemplified ion, 2173). Band 3-2, identified in lane 1 of the gel shown in Figure 1, is clearly labeled as containing complement component 3 precursor. Thus, it can be ascertained that the claimed SEQ ID NO:2 is a fragment of the complement C3 precursor protein weighing about 2173 daltons obtained from Band 3-2 of the gel as shown in Figure 1. Band 3-2 is immediately evident in all four normal samples (lanes 1-4, as read from the left, marked by circles) and clearly absent in all five diabetes Type II samples (lanes 5-9, marked by squares).

No new matter has been added; Figure 1, as attached, is simply a clearer copy of Figure 1 as originally filed and is provided to clarify the presence and differential expression of the claimed biopolymer markers (SEQ ID NOS:1 and 2). The gel shown in the figure does not represent new experimentation; the figure shows a clearer image of the original gel made at the time that the experiments described in the instant specification were first carried out.

5. The second figure attached hereto is entitled "HiQ3 (scrub) Normal vs. Diabetes Type II" and represents Figure 4 as

originally filed. This figure was also produced by scanning the original photograph of the gel. The claimed SEQ ID NO: 3 was obtained from samples analyzed in the gel shown in Figure 4.

At page 46, lines 13-15 of the instant specification as originally filed, SEQ ID NO:3 is identified as a fragment of the complement C3 precursor protein having a molecular weight of about 1191 daltons (1190.6210 daltons). Figure 5, as originally filed, shows the characteristic mass spectral profile of SEQ ID NO:3 (see top left of figure for band number analyzed, Q (SCRUB)S2 and see top right of figure for molecular weight of the exemplified ion, 1190.60). Band 2, identified in lane 10 of the gel shown in Figure 4, is clearly labeled as containing complement component 3 precursor. Thus, it can be ascertained that the claimed SEQ ID NO:3 is a fragment of the complement C3 precursor protein weighing about 1191 daltons obtained from Band 2 of the gel as shown in Figure 4. Band 2 is immediately evident in all four normal samples (lanes 7-10, as read from the left) and clearly absent in all five diabetes Type II samples (lanes 2-6). not clear. LVcook 2/17/06

No new matter has been added; Figure 4, as attached, is simply a clearer copy of Figure 4 as originally filed and is provided to clarify the presence and differential expression of one of the claimed biopolymer markers (SEQ ID NO:3). The gel shown in the figure does not represent new experimentation; the figure shows a clearer image of the original gel made at the time that the experiments described in the instant specification were first carried out.

6. The attached table is a partial listing of markers identified by the instant inventors; including the currently claimed markers, SEQ ID NOS:1-3 (see experiments 9, 10 and 17; marked by *). Each peptide marker in the table is described using five main categories. For example, one of the currently claimed markers, SEQ ID NO:2, was obtained from Band 3 of the gel using DEAE 1 Elution chromatography as the preparatory step to mass spectrometric analysis, identified during experiment 17 as a fragment of complement C3 precursor weighing about 2172 daltons and was found to be present in normal samples during comparison of normal samples versus Type II diabetes samples. It is noted that instantly claimed SEQ ID NO:1 was also identified in Band 5 of the gel shown in Figure 4. No new matter has been added by the disclosure of the table. The data summarized in the attached table does not represent new experimentation; the table shows the data which was collected at the time that the experiments described in the instant specification were first carried out.

7. Accordingly, it is established that the figures(Figures 1-5, as originally filed and Figures 1 and 4, as attached) show that the claimed peptides (SEQ ID NOS:1-3) are present in samples obtained from patients determined to be normal with regard to Type II diabetes and absent from samples obtained from Type II diabetes patients. Thus, contrary to the Examiner's determination, the figures do show differential expression of the claimed sequences (SEQ ID NOS:1-3).

The undersigned declares that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the Application or any patent issuing thereon.

1/26/2006
Date

Ferris H. Lander
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[redacted]

Experiment No.	Band No.	Preparatory Step	M.W. (daltons)	Sequence	Protein Source	Criteria	Designation	Docket
1	1	HIQ	1356		Fibronectin Precursor	IR vs NH	NH	2132.103
1	1	HIQ	1625		Fibronectin Precursor	IR vs NH	NH	2132.103
1	1	HIQ	1819		Fibronectin Precursor	IR vs NH	NH	2132.103
2	2	HIQ	1337		Inter Apha Trypsin Inhibitor	IR vs NH	NH	2132.105
2	2	HIQ	1583		Inter Apha Trypsin Inhibitor	IR vs NH	NH	2132.105
2	2	HIQ	1812		Inter Apha Trypsin Inhibitor	IR vs NH	NH	2132.105
3	4	HIQ	1817		Complement C3 Precursor	IR vs NH	NH	2132.102
3	4	HIQ	2755		Complement C3 Precursor	IR vs NH	NH	2132.102
5	7	HIQ	1287		Apolipopro tein A-IV Precursor	IR vs NH	NH	2132.101
5	7	HIQ	1311		Apolipopro tein A-IV Precursor	IR vs NH	NH	2132.101
5	7	HIQ	1908		Complement C3 Precursor	IR vs NH	NH	2132.102
5	7	HIQ	1367		Transthyretin	IR vs NH	NH	2132.106
6	3	HIQ			Betain/GAI BA transport	IR vs NH	IR	2132.097
6	3	HIQ	1208		Carnitine Octanoyl Transferase	IR vs NH	IR	2132.097
6	3	HIQ			HP AB051484	IR vs NH	IR	2132.099
6	3	HIQ			HP AL512706	IR vs NH	IR	2132.099
6	3	HIQ	1545		Macroglobulin Alpha 2	IR vs NH	IR	2132.099
6	3	HIQ	1211		Inter Apha Trypsin Inhibitor	IR vs NH	IR	2132.1
6	3	HIQ	1812		Inter Apha Trypsin Inhibitor	IR vs NH	IR	2132.1
6	6	HIQ	1199		Apoliporpotein	IR vs NH	NH	2132.101
6	6	HIQ	1226		Human Serum Albumin	IR vs NH	NH	2132.104
7	5	HIQ	1274		Globin (Beta, Hemo or Alpha)	IR vs NH	IR	2132.098
7	5	HIQ	1314		Globin (Beta, Hemo or Alpha)	IR vs NH	IR	2132.098
7	5	HIQ	1529		Globin (Beta, Hemo or Alpha)	IR vs NH	IR	2132.098
8	1	HIQ3	1630	seq ID NO: 3 ?	Fibronectin Precursor	T2 vs NH	NH	2132.109
* 9	2	HIQ3	1190		Complement C3 Precursor	T2 vs NH	NH	2132.108 *
10	5	HIQ3	1333	seq ID NO: 1	Apolipoprotein E	T2 vs NH	NH	2132.107
* 10	5	HIQ3	1211		Complement C3 Precursor	T2 vs NH	NH	2132.108 *
10	5	HIQ3	1497		Complement C3 Precursor	T2 vs NH	NH	2132.108
11	3	HIQ3	1199		Actin Beta	T2 vs NH	T2	2132.11 o
11	3	HIQ3	1104		Apolipopro tein A-IV Precursor	T2 vs NH	T2	2132.111
11	3	HIQ3	1353		Apolipopro tein A-IV Precursor	T2 vs NH	T2	2132.111
12	4	HIQ3	1970		Complement C3 Precursor	T2 vs NH	T2	2132.11°
13	6	HIQ3	1301		Proapoliprotein	T2 vs NH	T2	2132.11°
14	1	HIQ	1698		HP AK026417 / HP AL133517	IR vs NH	NH	2132.104
15	6	HIQ			Andrenergic Alpha 2 Receptor	IR vs NH	IR	2132.097
16	1	DEAE-1	1628		Fibronectin Precursor	T2 vs NH	NH	2132.109
16	1	DEAE-1	1912		Fibronectin Precursor	T2 vs NH	NH	2132.109
16	1	DEAE-1	1927		Fibronectin Precursor	T2 vs NH	NH	2132.109
17	3	DEAE-1	1624	seq ID NO: 1	ABC Transporter	T2 vs NH	NH	2132.107
* 17	3	DEAE-1	1211		Complement C3 Precursor	T2 vs NH	NH	2132.108 *
* 17	3	DEAE-1	2172		Complement C3 Precursor	T2 vs NH	NH	2132.108 *
18	4	DEAE-1	1552	seq ID NO: 2	HP AC024778	T2 vs NH	NH	2132.107
18	4	DEAE-1	1552		Synaptonemal Complex Prot. 2	T2 vs NH	NH	2132.107
18	4	DEAE-1	[illegible]		Fibrino[illegible]	T2 vs NH	NH	[illegible]